# Long-Term Hypoxia Maintains a State of Dedifferentiation and Enhanced Stemness in Fetal Cardiovascular Progenitor Cells.

**Journal:** Int J Mol Sci

**Publication Year:** 2021

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**PubMed link:** 34502291

**Funding Grants:** Stem Cell Scholars- from Basic Research to Clinical Translation: training a diverse pool of students in the lab, engaging them in patient and healthcare activities, motivating them to educate their immediate community and enabling them for careers in ...

**Public Summary:**
Early-stage mammalian embryos survive within a low oxygen tension environment and develop into fully functional, healthy organisms despite this hypoxic stress. This suggests that hypoxia plays a regulative role in fetal development that influences cell mobilization, differentiation, proliferation, and survival. The long-term hypoxic environment is sustained throughout gestation. Elucidation of the mechanisms by which cardiovascular stem cells survive and thrive under hypoxic conditions would benefit cell-based therapies where stem cell survival is limited in the hypoxic environment of the infarcted heart. The current study addressed the impact of long-term hypoxia on fetal Islet-1+ cardiovascular progenitor cell clones, which were isolated from sheep housed at high altitude. The cells were then cultured in vitro in 1% oxygen and compared with control Islet-1+ cardiovascular progenitor cells maintained at 21% oxygen. RT-PCR, western blotting, flow cytometry, and migration assays evaluated adaptation to long term hypoxia in terms of survival, proliferation, and signaling. Non-canonical Wnt, Notch, AKT, HIF-2α and Yap1 transcripts were induced by hypoxia. The hypoxic niche environment regulates these signaling pathways to sustain the dedifferentiation and survival of fetal cardiovascular progenitor cells.

**Scientific Abstract:**
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